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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,573	02/28/2002	Theodorus Petrus Maria Schetters	I 2001.004 US	3895

31846 7590 07/14/2004

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,573	SCHETTERS ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-35 and 64-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-35 and 64-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

L. F. S.
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicant's amendment filed on filed on 4/20/04is acknowledged.

Status of claims

2. Claims 32-35 and 64-67 are pending in the application.

Claims 32 and 66 have been amended.

Specification Informalities withdrawn

3. In view of the amendment of record, the specification informalities are withdrawn.

Claim Rejections - 35 USC § 101 withdrawn

4. In view of amendment to the claims, the rejection claims 32-35 and 64-67 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn.

Rejections - 35 USC 112, second paragraph withdrawn

5. In view of amendment to the claims, the rejection of claims 32-35 and 64 –67 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC § 102 *withdrawn*

6. In view of arguments of record the rejection of claims 32-35 and 64 under 35 U.S.C. 102(b) as being anticipated by Kulakov et al 1998 is withdrawn.

Claim Rejections - 35 USC 112, first paragraph maintained

7. The written description rejection of claims 32-35 and 64 under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention is maintained as set forth in the previous office action.

The claims are directed to a Babesia canis associated protein said protein having a molecular weight of 15 kD and comprising an amino acid sequence that is at least 80%, 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 or an immunogenic fragment of said protein. Claims are also directed to a vaccine for combating Babesia canis infections comprising a nucleic acid sequence encoding a protein having a molecular weight of 15 kD and comprising an amino acid sequence that is at least 80% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 or an immunogenic fragment of said protein, a pharmaceutically acceptable carrier, an adjuvant and an additional protein derived from a virus or microorganism pathogenic to dogs or a nucleic acid sequence encoding said antigen wherein said virus or micro-organism pathogenic to dogs is selected from the group of Ehrlichia canis, Babesia gibsoni, vogeli, rossi, Leishmania donovan complex, Canine parvovirus, Canine distempervirus, Leptospira interrogans serovar canocola icterohaemorrhagiae, pomona, grippotyphosa , grippotyphosa, bratislava, Canine hepatitisvirus. Canine parainfluenzavirus, rabies virus, Hepatozoon canis and Borrelia burgdorfiri.

The specification discloses a recombinant Babesia canis protein having 15KD molecular weight and comprising the amino acid sequence as set forth in SEQ.ID.NO: 2. However, the specification does not disclose

(1) Babesia canis protein having a molecular weight 15KD and comprising an amino acid sequence that is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an
immunogenic fragments of said protein

(2) A vaccine for combating B.canis infection comprising a Babesia canis protein having a molecular weight of 15KD and comprising an amino acid sequence that is at least 80%, homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an Immunogenic fragments of said protein (the examiner is considering these as a variants and address them as variants hereafter in the action)

Therefore, or said variants do not meet the guidelines on written description.

The specification fails to disclose any substitution, insertion or deletion or change in (i) a in a protein SEQ.ID.NO: 2 to obtain a variants having 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: or immunogenic functional fragments, (ii) a vaccine comprising said variants or a nucleic acid encoding said variants and an additional protein derived from a virus or microorganism pathogenic to dogs or a nucleic acid sequence encoding said antigen wherein said virus or micro-organism pathogenic to dogs is selected from the group of Ehrlichia canis, Babesia gibsoni, vogeli, rossi, Leiahmania donovan complex, Canine parvovirus, Canine distempervirus, Leptospira interrogans serovar canocola icterohaemorrhagiae, pomona, grippotyphosa , grippotyphosa, bratislava, Canine hepatitisvirus. Canine parainfluenzavirus, rabies virus, Hepatozoon canis and Borrelia burgdorfiri.

The specification does not describe any variants in vaccine preparations for combating B.canis infection in dogs. None of the above variants and their use in a vaccine preparation meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now

claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach variants sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

8. The rejection of claims 32-35 and 64 [illegible] under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated Babesia canis associated protein 15kD, SEQ.ID.NO: 2 and a vaccine composition comprising said isolated protein does not reasonably provide enablement for Babesia canis protein having a molecular weight 15KD is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein is maintained as set forth in the previous office action.

The nature of the disclosed invention is relates to cloning of nucleic acid sequences encoding a novel Babesia canis associated proteins from B.canis isolate A and B from France that are useful for diagnostic tools for the detection of Babesia canis and for a vaccine composition against B.canis homologous strains
The specification on pages 19-36 indicates that the claimed protein may be used as diagnostic reagent and a vaccine composition against homologous B.canis infections. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein. Any substitution, insertion or deletion or change in a peptide encoded by a nucleotide sequence of SEQ.ID.NO: 2 are highly complex and unpredictable. As taught by the prior art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide. Furthermore, it is unclear whether protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein can be used as diagnostic reagent or in a vaccine composition. Thus, protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein at protein level or nucleotide level and fragments must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein because it fails to provide guidance protein that vary by 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or an immunogenic fragments of said protein is related to anti-microbial action

and its use in diagnostic or prophylactic reagent. The specification provides no disclosure how a protein variant of SEQ.ID.NO: 2 may be used as a vaccine because it fails to provide guidance whether this variant has the ability to induce a protective immune response or to bind to antisera from infected animal. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Applicant's arguments filed on 4/20/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the specification disclose antigenic fragments of SEQ.ID.NO: 2 and brings examiner's attention to the specification (pages 7-10, 11 and 29-30) and states that the specification has disclosed the claimed fragments and those of ordinary skill in the art knows different fragments of a protein Further applicant states linear epitopes present a certain molecular structure to the immune system and trigger an array of immune response. Applicant states that the references cited by the examiner such as Burgess are not relevant and keep on explaining to the examiner about the mutations, epitopes etc (in pages 8-12 of the response). The examiner disagrees with the applicant because the specification does not disclose an isolated comprising antigenic fragment of the polypeptide sequence as set forth in SEQ.ID.NO: 2. The specification teaches an isolated polypeptide consisting of antigenic fragment of SEQ.ID.NO: 2. Further examiner understands that while different fragments are recognized by those of ordinary skill in the art, the claimed homologous and immunogenic fragments require undue experimentation to practice as claimed because the transitional limitation "comprises" similar to the limitations, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See *Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App.1948)* ("comprising"

leaves the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting of represents closed claim language and excludes any element, step, or ingredient not specified in the claim. In *re Gray, 53 F. 2d 520, Il USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).* Therefore, the fragments as claimed are not supported by the specification. Hence the references cited by the examiner are properly applicable to the scope rejection.

The examiner would like to point to the applicant that fragments as claimed are not shorter than SEQ.ID.NO: 2 because applicant is claiming isolated polypeptide comprising (open language) antigenic fragment of SEQ.ID.NO: 2 and thus claiming an isolated polypeptide comprising a fragment of SEQ.ID.NO: 2 plus unlimited and unknown amino acid sequences without any function. Thus, the fragments as claimed are broader than the claimed SEQ.ID.NO: 2. Please note applicant is not claiming an isolated polypeptide consisting of antigenic fragment as set forth in SEQ.ID.NO: 2. The examiner is aware of linear epitopes and their use in immunology art. An isolated protein or polypeptide consists of several linear epitopes that are functional. Therefore, this rejection is maintained.

Claim objections maintained

9. The objection to claims 65-67 as being depended from canceled claims 36 and 38 is maintained as set forth in the previous office action.

Applicant states 11/17/03, the claim dependency has been corrected.

Please note the latest amendment filed on 4/20/04 does not indicate that the claims have been corrected. Therefore, applicant is advised to amend the claims in the next response to this office action.

Claim Rejections - 35 USC § 102 maintained.

10. The rejection of claims 32-35 and 64 –65 under 35 U.S.C. 102(b) as being anticipated by Schetters et al 1992 (PARASITE IMMUNOLOGY 1992, 14(3) 295-305 abstract only) is maintained as set forth in the previous office action.

Schetters et al disclose a vaccine comprising Babesia associated protein in culture supernatants of Babesia canis in the adjuvant (see abstract). In the absence of evidence to the contrary the disclosed prior art culture supernatants comprises B.canis associated protein 15KD antigen. Characteristic such as SEQ.ID.NO: 2 is considered as an inherent property of the disclosed culture supernatants. Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. Thus the prior art anticipated the claimed invention.

Applicant's arguments filed on 4/20/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the assignee of the application and of the patent that originated from the teachings of the Schetler article are one in the same, Akzo Nobel. The proteins in the supernatant are exo-antigen and are the subject of US patent 6,045,806. Applicant further describes the differences between the two proteins. The exo-antigens of the prior art are not recognized by an antiserum specific for 15kD antigen of the invention. Therefore, Bcvir15 is not an exoantigen.

The examiner has rejected the claims based on the language (open language such as having, comprising etc) used in the claims. As the claim recites an isolated protein " having" or "an immunogenic fragment of said protein" read on the prior art because applicant is not claiming the protein by its reactivity to antisera raised 15kD antigens but broadly claiming any isolated protein having an amino acid sequence that is homologous to SEQ.ID.NO: 2. Therefore, any two amino acids of the prior art read on the claimed invention. Further, the

limitations which applicant is arguing are not set forth in the claims. Therefore, the rejection is maintained.

Remarks

11. No claims are allowed.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

13. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

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